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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,246	03/17/2005	Byong-Sung Kwak	20345/0202513-US0	2511
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DARBY & DARBY P.C. P.O. BOX 770 Church Street Station New York, NY 10008-0770			EXAMINER OH, TAYLOR V	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/528,246	KWAK ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Taylor Victor Oh	1625	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 17 March 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 March 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/17/05</u> .   | 6) <input type="checkbox"/> Other: _____                          |

**The Status of Claims:**

Claims 1-16 are pending.

Claims 1-16 are rejected.

**DETAILED ACTION**

**Priority**

1. It is noted that this application is a 371 of PCT/KR02/01775 (09/18/2002).

**Drawings**

2. The drawing filed on 3/17/05 is accepted by the examiner.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4, and 6-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using nickel, palladium, platinum, rhodium, iridium, ruthenium, osmium as the metal catalyst, does not reasonably provide enablement for using any metal catalysts generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

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connected, to include all kinds of metal catalysts unrelated to the claimed invention commensurate in scope with these claims.

Furthermore, the instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without **undue experimentation**.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation, citing *Ex Parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction or guidance provided,
- 3) the presence or absence of working examples,
- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art,
- 7) the predictability of the art, and
- 8) the breath of the claims.

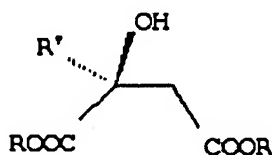
#### **The Nature of the Invention**

The nature of the invention in claim 1 is described below:

Claim 1. (original): A continuous process for the production of chemically pure (S)- $\beta$ -hydroxy- $\gamma$ -butyrolactone having desired optical activity, which comprises:

a) dissolving carboxylic acid ester derivative having the following Formula 2 in solvent at an amount of 2-50 wt%, the solvent being added with an organic or inorganic acid;

Formula 2



b) subjecting the carboxylic acid ester derivative solution to hydrogenation at 50-500 °C under a pressure of 15-5,500 psig at weight-hourly-space-velocity of 0.1-10 h<sup>-1</sup>, in a fixed bed reactor charged with a metal catalyst-impregnated inorganic oxide support, a molar ratio of hydrogen to carboxylic acid ester derivative ranging from 2 to 10; and

#### The State of the Prior Art

The states of the prior art are described as followed:

In U.S. Pat. No. 5,998,633, there is disclosed a production process for the preparation of a substituted  $\gamma$ -butyrolactone by oxidizing a carbohydrate, yielding an acetonide intermediate, which is treated with an inorganic acid (HCl aqueous solution). This technique suffers from a complexity of the reaction mechanism and the generation

of large quantities of waste, and thus is difficult to apply industrially.

In U.S. Pat. No. 6,122,122 there is disclosed a method for the production of (S)- $\beta$ -hydroxy- $\gamma$ -butyrolactone having high optical purity, comprising reacting amylopectin using an enzyme to afford an oligosaccharide which is then reacted with an alkaline anionic exchange resin and an oxidizing agent, to obtain (S)-3,4-dihydroxy-butyric acid, which is desorbed and subjected to esterification and cyclization. However, this method is disadvantageous in terms of low preparation yield due to a complexity of the reaction mechanism, and high cost is problematic when applied on the large scale.

In U.S. Pat. No. 5,808,107, there is disclosed a process for producing (S)- $\beta$ -hydroxy- $\gamma$ -butyrolactone by reducing L-malic acid dimethyl ester with lithium chloride and sodium borohydride, to afford (S)-3,4-dihydroxybutyric acid, which is then treated with an acid (HCl) in a methanol solvent. According to the above patent, the optical purity is maintained during the reaction. However, this process is environmentally harmful, and has shortcomings attributable to a complicated batch type preparation method. Furthermore, the use of high-priced explosive reducing agent makes the process unfeasible in the aspect of cost. Hence, the above process is unsuitable for preparation on a large scale. Also, ether used as a reaction solvent is harmful to the human body when used in large amounts, and is explosive.

Kwak et al (WO 02/10147) discloses the following process as shown below:

hydrogenation of esters of substituted carboxylic acids into optically pure (S)-beta-hydroxy-gamma-butyrolactone in the presence of a catalyst in a fixed bed reactor. By virtue of its superior production yield and productivity, this continuous process is far more economical than conventional processes. The process of the present invention also has an economical benefit in that the catalyst can be recovered and used repeatedly. Additionally, the above process requires no complicated post-processes, such as filtering off of the catalyst.

palladium (Pd), platinum (Pt), rhodium (Rh), iridium (Ir), ruthenium (Ru), osmium (Os) and mixtures thereof. Such catalytically effective ingredient is impregnated on a support, which is preferably selected from the group consisting of alumina, silica, silica-alumina, zirconia, titania, zeolite and a molecular sieve.

As the prior art have been discussed in the above, there is no conclusive data that all kinds of metal catalysts would be required to produce the final desired product except some metal hydrogenation catalyst, nickel, palladium, platinum, rhodium, iridium, ruthenium, osmium.

**The predictability or lack thereof in the art**

In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that not every metal catalyst would work on the claimed process in the same way as do those metal catalysts such as nickel, palladium, platinum, rhodium, iridium, ruthenium, osmium disclosed in the specification.

Furthermore, the specification of the claimed invention does support the very idea of the unpredictable aspect of the catalysts by disclosing those specific and workable metal catalysts (see pages 6 and 9, lines, 6-10 and 9-11) for the metal hydrogenation catalyst in the above, not that all kinds of the metal catalyst known in the art will work.

Moreover, chemical reactions are well-known to be unpredictable, *In re Marzocchi*, 169 USPQ 367, *In re Fisher*, 166 USPQ 18. Additionally, catalytic processes, such as are present here, are inherently unpredictable. The U.S. District Court District of Connecticut held in *MOBIL OIL CORPORATION v. W.R. GRACE & COMPANY*, 180 USPQ 418 that "there is an inherent mystery surrounding the unpredictability of the performance of catalysts; a mystery which is generally recognized and acknowledged by chemists in the cracking art. This is one more reason why the presumption of patent validity "should not be disregarded especially in a case of this sort where the intricate questions of [bio]chemistry involved are peculiarly within the particular competence of the experts of the Patent Office." *Merck & Co. v. Olin Mathieson Chemical Corp.*, 253 F.2d 156, 164, 116 USPQ 484, 490 (4th Cir. 1958)". "The catalytic action can not be forecast by its chemical composition, for such action is not understood and is not known except by actual test, *Corona Cord Tire Co. v. Dovan*



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*Chemical Corp.*, 276 U.S. 358, 368-369 (1928). Also see, *Application of Grant*, 304 F.2d 676, 679, 134 USPQ 248, 250-251 (CCPA 1962); *Rich Products Corp. v. Mitchell Foods, Inc.*, 357 F.2d 176, 181, 148 USPQ 522, 525-526 (2d Cir. 1966), cert. denied 385 U.S. 821, 151 USPQ 757 (1966); *Ling-Temco-Vought, Inc. v. Kollsman Instrument Corp.*, 372 F.2d 263, 268, 152 USPQ 446, 450-451 (2d Cir. 1967); *Georgia-Pacific Corp. v. United States Plywood Corp.*, 258 F.2d 124, 132-133, 118 USPQ 122, 128-129."

Therefore, from the above, it is clear that the use of every generic "metal catalyst" will not form the desired claimed product in a good yield.

#### **The amount of direction or guidance present**

The direction present in the instant specification is that not any metal catalyst can be led to the formation of the desired product. According to the specification, it is silent as to how any metal catalyst can be led to the formation of the desired product and fails to provide guidance as to whether any acidic catalyst is sufficient enough to allow to form the desired product in sufficient quantities; the specification fails to provide a correlation between the claimed process of the invention and the functional language of any metal catalyst.

#### **The presence or absence of working examples**

In the instant case, the claim encompasses all the various metal catalysts. Applicants' specification provide only one particular exemplified catalyst compound Ru as shown in the example for producing the desired compound in the specification.

However, this can not be the representatives for all the metal catalysts which would work for the claimed process. Thus, the specification fails to provide enough working examples as to how other types of metal catalysts can be resulted in the claimed products, i.e. again, there is no correlation between the functional language of any metal catalyst and the desired final product.

#### **The breadth of the claims**

The breadth of the claims is that any metal catalyst would work on the claimed process in the same way as those disclosed catalyst in the specification without considering the affect or impact of the different types of metal catalysts on the reactants.

#### **The quantity of experimentation needed**

The quantity of experimentation needed is large. One of skill in the art would need to determine which one of the metal catalysts would be capable of forming the desired product and would furthermore then have to determine which one of the metal catalysts would not be resulted in the claimed desired compounds in a sufficient quantity.

#### **The level of the skill in the art**

Even though the level of skill in the art of hydrogenation process is high, the skilled artisan employing this process would be a BS Chemist working in a laboratory facility. He would know how to use the taught metal catalyst, but not how to select other catalyst without trial and error.

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which metal catalyst can be employed to produce the desired claimed compound encompassed in the instant claims, with no assurance of success.

Claim 16 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using formic acid, oxalic acid, malic acid, acetic acid, nitric acid, sulfuric acid, phosphoric acid, hydrochloric acid as the acidic catalyst, does not reasonably provide enablement for using any acidic catalysts generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to include all kinds of acidic catalysts unrelated to the claimed invention commensurate in scope with these claims.

Furthermore, the instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation, citing *Ex Parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

- 1) the quantity of experimentation necessary,

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- 2) the amount of direction or guidance provided,
- 3) the presence or absence of working examples,
- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art,
- 7) the predictability of the art, and
- 8) the breath of the claims.

#### **The Nature of the Invention**

The nature of the invention in claim 16 is described below:

Claim 16. (original): The process as defined in claim 2, further comprising removing carboxylic acid capable of being present in the hydrogenation products of the step b) through esterification with alcohol in the presence of an acid catalyst prior to the step c).

#### **The State of the Prior Art**

The states of the prior art are described as followed:

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In U.S. Pat. No. 5,998,633, there is disclosed a production process for the preparation of a substituted  $\gamma$ -butyrolactone by oxidizing a carbohydrate, yielding an acetonide intermediate, which is treated with an inorganic acid (HCl aqueous solution). This technique suffers from a complexity of the reaction mechanism and the generation

of large quantities of waste, and thus is difficult to apply industrially.

In U.S. Pat. No. 6,122,122 there is disclosed a method for the production of (S)- $\beta$ -hydroxy- $\gamma$ -butyrolactone having high optical purity, comprising reacting amylopectin using an enzyme to afford an oligosaccharide which is then reacted with an alkaline anionic exchange resin and an oxidizing agent, to obtain (S)-3,4-dihydroxy-butyric acid, which is desorbed and subjected to esterification and cyclization. However, this method is disadvantageous in terms of low preparation yield due to a complexity of the reaction mechanism, and high cost is problematic when applied on the large scale.

In U.S. Pat. No. 5,808,107, there is disclosed a process for producing (S)- $\beta$ -hydroxy- $\gamma$ -butyrolactone by reducing L-malic acid dimethyl ester with lithium chloride and sodium borohydride, to afford (S)-3,4-dihydroxybutyric acid, which is then treated with an acid (HCl) in a methanol solvent. According to the above patent, the optical purity is maintained during the reaction. However, this process is environmentally harmful, and has shortcomings attributable to a complicated batch type preparation method. Furthermore, the use of high-priced explosive reducing agent makes the process unfeasible in the aspect of cost. Hence, the above process is unsuitable for preparation on a large scale. Also, ether used as a reaction solvent is harmful to the human body when used in large amounts, and is explosive.

Kwak et al (WO 02/10147) discloses the following process as shown below:

hydrogenation of esters of substituted carboxylic acids into optically pure (S)-beta-hydroxy-gamma-butyrolactone in the presence of a catalyst in a fixed bed reactor. By virtue of its superior production yield and productivity, this continuous process is far more economical than conventional processes. The process of the present invention also has an economical benefit in that the catalyst can be recovered and used repeatedly. Additionally, the above process requires no complicated post-processes, such as filtering off of the catalyst.

palladium (Pd), platinum (Pt), rhodium (Rh), iridium (Ir), ruthenium (Ru), osmium (Os) and mixtures thereof. Such catalytically effective ingredient is impregnated on a support, which is preferably selected from the group consisting of alumina, silica, silica-alumina, zirconia, titania, zeolite and a molecular sieve.

As the prior art have been discussed in the above, there is no conclusive data that all kinds of acidic catalysts would be required to produce the final desired product except some acidic catalyst, hydrochloric acid.

**The predictability or lack thereof in the art**

In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that not every any acidic catalyst would work on the claimed process in the same way as do those catalysts such as formic acid, oxalic acid, malic acid, acetic acid, nitric acid, sulfuric acid, phosphoric acid, hydrochloric acid disclosed in the specification. For example, Gardener (US 3,878,261) discloses the super acid catalyst of  $\text{SbF}_5$  and  $\text{CF}_3\text{SO}_3\text{H}$  used for isomerizing paraffins containing 4 to 12 carbons in a feed stream (see abstract page ); furthermore, according to the textbook, March's Advanced Organic Chemistry (March et al, 4<sup>th</sup> ed. 1992), another super acid,  $\text{FSO}_3\text{H-SbF}_6$ , is used in the formation of a carbocation, such as tert-butyl cation (see p. 219, the fourth paragraph) from isobutane unlike the claimed process.

Furthermore, the specification of the claimed invention does support the very idea of the unpredictable aspect of the catalysts by disclosing those specific and workable catalysts (see page 8, line 24 to page 9, line 2) for the process in the above, not that all kinds of the acidic catalyst known in the art will work.

Moreover, chemical reactions are well-known to be unpredictable, *In re Marzocchi*, 169 USPQ 367, *In re Fisher*, 166 USPQ 18. Additionally, catalytic processes, such as are present here, are inherently unpredictable. The U.S. District Court District of Connecticut held in *MOBIL OIL CORPORATION v. W.R. GRACE & COMPANY*, 180 USPQ 418 that "there is an inherent mystery surrounding the unpredictability of the performance of catalysts; a mystery which is generally recognized and acknowledged by chemists in the cracking art. This is one more reason why the

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presumption of patent validity "should not be disregarded especially in a case of this sort where the intricate questions of [bio]chemistry involved are peculiarly within the particular competence of the experts of the Patent Office." *Merck & Co. v. Olin Mathieson Chemical Corp.*, 253 F.2d 156, 164, 116 USPQ 484, 490 (4th Cir. 1958)".

"The catalytic action can not be forecast by its chemical composition, for such action is not understood and is not known except by actual test, *Corona Cord Tire Co. v. Dovan Chemical Corp.*, 276 U.S. 358, 368-369 (1928). Also see, *Application of Grant*, 304 F.2d 676, 679, 134 USPQ 248, 250-251 (CCPA 1962); *Rich Products Corp. v. Mitchell Foods, Inc.*, 357 F.2d 176, 181, 148 USPQ 522, 525-526 (2d Cir. 1966), cert. denied 385 U.S. 821, 151 USPQ 757 (1966); *Ling-Temco-Vought, Inc. v. Kollsman Instrument Corp.*, 372 F.2d 263, 268, 152 USPQ 446, 450-451 (2d Cir. 1967); *Georgia-Pacific Corp. v. United States Plywood Corp.*, 258 F.2d 124, 132-133, 118 USPQ 122, 128-129."

Therefore, from the above, it is clear that the use of every generic "an acidic catalyst" will not form the desired claimed product in a good yield.

#### **The amount of direction or guidance present**

The direction present in the instant specification is that not any acidic catalyst can be led to the formation of the desired product. According to the specification, it is silent as to how any acidic catalyst can be led to the formation of the desired product and fails to provide guidance as to whether any acidic catalyst is sufficient enough to allow to form the desired product in sufficient quantities; the specification fails to



provide a correlation between the claimed process of the invention and the functional language of any acidic catalyst.

**The presence or absence of working examples**

In the instant case, the claim encompasses all the various acidic catalysts. Applicants' specification provide only three particular exemplified catalyst compounds, formic acid, oxalic acid, nitric acid as shown in the examples 3-5 for producing the desired compound in the specification. Thus, the specification fails to provide working examples as to how other types of acidic catalysts can be resulted in the claimed products, i.e. again, there is no correlation between the functional language of any acidic catalyst and the desired final product.

**The breadth of the claims**

The breadth of the claims is that any acidic catalyst would work on the claimed process in the same way as those disclosed catalyst in the specification without considering the affect or impact of the different types of acidic catalysts on the starting compounds; for example, the super acid  $\text{FSO}_3\text{H-SbF}_6$  disclosed in March's Advanced Organic Chemistry (March et al, 4<sup>th</sup> ed. 1992) has a high likelihood of removing hydrogen ions from either of the reactants, hydrogenation products and alcohol instead of helping them to form the desired product, thereby detrimentally affecting the yield of the desired final product.

**The quantity of experimentation needed**

The quantity of experimentation needed is large. One of skill in the art would need to determine which one of the acidic catalysts would be capable of forming the

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desired product and would furthermore then have to determine which one of the acidic catalysts would not be resulted in the claimed desired compounds in a sufficient quantity.

**The level of the skill in the art**

Even though the level of skill in the art of esterification is high, the skilled artisan employing this process would be a BS Chemist working in a laboratory facility. He would know how to use the taught acid catalyst, but not how to select other catalyst without trial and error.

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which acidic catalyst can be employed to produce the desired claimed compound encompassed in the instant claims, with no assurance of success.

Claims 2 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a sulfonate-substituted resin as a solid catalyst, this does not reasonably provide enablement for all kinds of solid catalysts known in the art. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to include all kinds of solid catalysts unrelated to the claimed invention commensurate in scope with these claims.

Furthermore, the instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without **undue experimentation**. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation, citing *Ex Parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction or guidance provided,
- 3) the presence or absence of working examples,
- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art,
- 7) the predictability of the art, and
- 8) the breadth of the claims.

#### **The Nature of the Invention**

The nature of the invention in claims 2 and 14 are shown below:

Claim 2. (original): A continuous process for the production of chemically pure (S)- $\beta$ -hydroxy- $\gamma$ -butyrolactone having desired optical activity, which comprises:

- a) dissolving carboxylic acid ester derivative having the following Formula 2 in solvent at an amount of 2-50 wt%, the solvent being added with an organic or inorganic acid;

b) subjecting the carboxylic acid ester derivative solution to hydrogenation at 50-500 °C under a pressure of 15-5,500 psig at weight-hourly-space-velocity of  $0.1-10 \text{ h}^{-1}$ , in a fixed bed reactor charged with a metal catalyst-impregnated inorganic oxide support to give hydrogenation products containing an intermediate having the following Formula 3 and (S)- $\beta$ -hydroxy- $\gamma$ -butyrolactone having the following Formula 4, a molar ratio of hydrogen to carboxylic acid ester derivative ranging from 2 to 10; and

c) subjecting the hydrogenation products to cyclization in the presence of a solid acid catalyst, whereby the intermediate present therein is converted into (S)- $\beta$ -hydroxy- $\gamma$ -butyrolactone; and

Claim 14. (currently amended): The process as defined in claim 1 or 2, wherein the carboxylic acid ester derivative is obtained by reacting carboxylic acid with a linear, cyclic or aromatic alcohol having 1-10 carbon atoms in the presence of a solid acid catalyst, under conditions of a temperature of 50-150 °C, a pressure of 1.0-300 psig and weight-hourly-space-velocity of  $0.1-10 \text{ h}^{-1}$ , in which the alcohol is used at an amount of 2.0-40 equivalents based on the carboxylic acid.

### **The State of the Prior Art**

The states of the prior art are described as followed:

Choudhary et al (US 6,420,596) discloses the process for the esterification of tertiary alcohol by an acid anhydride using a solid catalyst comprising halides of indium, gallium, zinc, and iron.

Abe et al (US 5,703,272) discloses the process for preparing a carboxylic acid ester by subjecting a carboxylic acid and an alcohol in the presence of a silica titania catalyst.

Harrison et al (US 5,536,856) discloses the esterification process to be carried out in the presence of an ion exchange resin containing sulfonic group and carboxylic group.

Onoda et al (US 4,018,816) discloses the preparation of methacrylate by reacting methacrylic acid and alcohol in the presence of an solid catalyst containing a silica titania catalyst.

As the prior art have been discussed in the above, there is no conclusive data that all the kinds of solid catalyst would work to produce the final desired product for the process except the presence of some the silica titania catalyst, the ion exchange resin containing sulfonic group and carboxylic group, solid catalyst comprising halides of indium, gallium, zinc, and iron.

#### **The predictability or lack thereof in the art**

In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that any solid catalyst would not work on the claimed process in the same way as the sulfonate-substituted resin disclosed in the specification.

According to T.P.Hilditch, the author of the "Catalytic Processes in Applied Chemistry" (see pages Xiii-XV, 1929), there is a definitive reason for an unpredictable aspect of the catalysts in the art of organic chemistry. T.P.Hilditch expressly teaches that any catalyst would not work for any kind of the reaction process; for example, the

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specific catalysts such as mineral acids, acetic anhydride , sulfuric acid, calcium chloride, and etc can be used for the esterification; on the other hand, this same kind of catalyst will not apply to the other types of the reaction process in the followings: the chlorination of organic compounds, the oxidation of organic compounds, the process for rubber accelerators, the hydrogenation or the dehydrogenation processes, ammonia synthesis, ammonia oxidation , sulfuric acid manufacture, and etc. (see pages Xiii-XV).

Furthermore, the specification of the claimed invention does support the very idea of the unpredictable aspect of the catalysts by disclosing the following specific , workable catalyst for the oxidation , not all kinds of the catalyst known in the art.

Moreover, the case law advocates that the catalyst compositions represent an unpredictable aspect in the art of organic chemistry . See Exparte Sizto, 9 USPQ2d 2081 (Bd. Of App. And Inter. March 1988). Therefore, the use of a generic phrase “a catalyst” can not ensure to form the desired claimed product in a good yield.

#### **The amount of direction or guidance present**

The direction present in the instant specification is that not any solid catalyst can be led to the formation of the desired product. According to the specification, it is silent as to how any solid catalyst can be led to the formation of the desired product and fails to provide guidance as to whether any solid catalyst is sufficient enough to allow to form the desired product in sufficient quantities; the specification fails to provide a

correlation between the claimed process of the invention and the functional language of any solid catalyst .

#### **The presence or absence of working examples**

There is only 1 working example using the sulfonate-substituted resin catalyst composition for producing the desired compound in the specification. This can not be the representatives for all the catalysts which would work for the claimed process. Thus, the specification fails to provide enough working examples as to how the other types of catalysts can be resulted in the claimed products, i.e. again, there is no correlation between the functional language of any solid catalyst and the desired final product.

#### **The breadth of the claims**

The breadth of the claims is that any solid catalyst would work on the claimed process in the same way as the disclosed catalyst without considering the affect or impact of the different catalysts on the starting compound , thereby affecting the yield of the desired final product.

#### **The quantity of experimentation needed**

The quantity of experimentation needed is large. One of skill in the art would need to determine which one of the solid catalysts would be capable of forming the desired product and would furthermore then have to determine which one of the solid catalysts would not be resulted in the claimed desired compounds in a sufficient quantity.

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which solid catalyst can be employed to produce the desired claimed compound encompassed in the instant claims, with no assurance of success.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1 and 2, the term "derivative" is recited. This is vague and indefinite because the specification does not elaborate what is meant by the term "derivative".

Therefore, an appropriate correction is required.

In claims 1,2 and 14, the phrases "R represents linear, cyclic alkyls or aryl groups of from 1 to 10 carbon atoms" and "carboxylic acid with a linear, cyclic alkyls or aromatic alcohol having 1 to 10 carbon atoms" are recited. These are vague and indefinite because the cyclic alkyl group requires at least 3 carbon atoms instead of 1 or 2 carbon atoms and the aromatic alcohol requires at least 3 carbon atoms instead of 1-5 carbon atoms. Therefore, an appropriate correction is required.



***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 7, 9, 12, and 14 are rejected under 35 U.S.C. 102(a) as being anticipated clearly by Kwak et al (WO 02/10147 A1).

Kwak et al discloses the continuous process for producing optically pure (s)-beta-hydroxy-gamma-butyrolactone in the following abstract (see abstract page):

(57) Abstract: Disclosed is a process for the production of optically pure (S)-beta-hydroxy-gamma-butyrolactone through the hydrogenation of substituted carboxylic acid derivatives. A solution containing 1 to 50 % by weight of a substituted carboxylic acid derivative is fed at a WHSV of 0.1 to 10 h<sup>-1</sup>, to a fixed bed reactor which is filled with a catalyst and maintained at a reaction temperature of 50 to 550 °C under a halogen partial pressure of 15 to 5,500 psig. The catalyst is composed of a noble metal as a catalytically effective ingredient which is impregnated in an inorganic oxide as a support. The molar ratio of the hydrogen to the substituted carboxylic acid derivative is maintained at a molar ratio of 1:1 to 10:1. The process can produce optically pure (S)-beta-hydroxy-gamma-butyrolactone with higher purities at higher yields than can conventional techniques. In addition to being relatively simple and environmentally friendly, the process is so economically favorable as to apply to industrial production.

**EXAMPLE 1**

**Preparation of Catalyst**

resulting ruthenium-supported catalyst was sintered at 550 °C for 6 hours under the air atmosphere in a muffle furnace. The catalyst was found to have a ruthenium content of 3.0 % by weight as measured by fluorescent X-ray analysis.

(see page 12, the first paragraph).

#### Examples of suitable noble metal catalyst

include Ni, Pd, Pt, Rh, Ir, Ru, Os and mixtures thereof with preference to Ru. The catalytically active ingredient may be used in a bare form or in a combination with a support. In the latter case, the noble metal is impregnated on the support. Suitable as a support is an inorganic oxide selected from the group consisting of alumina, silica, silica-alumina, zirconia, titania, zeolite and molecular sieves. Of them, silica is most preferred.

(see page 9, the first paragraph).

#### Continuous Preparation of Dimethyl (S)-Malate

In an automatic high-pressure reactor made of stainless steel 316 was filled 25 g of a solid acid catalyst. After being purged with nitrogen, the inside of the reactor was heated from room temperature to 84 °C and maintained at a pressure of 100 psig. L-malic acid was dissolved in 8 equivalents of methanol and the resulting solution was fed at a WHSV of 4.0 h<sup>-1</sup> into the reactor to produce the title compound at a yield of 90 %: Conversion 99 %. Selectivity 99 %.

(see page 12, the second paragraph).

The effluent from the reactor was distilled in vacuum to separate at a separation yield of 90 % dimethyl (S)-malate which was 99.8 % in purity and 99.9 % in optical purity. The preparation could be effected in a batch type. In this case, the reaction period of time was set to be 2 to 4 hours.

(see page 12, the first paragraph).

#### Continuous Preparation of (S)-Beta-Hydroxy-Gamma-Butyrolactone

In an automatic, stainless-steel 316, high pressure reactor (inner diameter 2.52 cm x length 60 cm) was filled 50 g of the catalyst prepared in Example 1. The catalyst was converted to a reduced state by raising the temperature at a rate of 1 °C per min to 350 °C and maintained at this temperature for 6 hours in a hydrogen atmosphere. After being cooled, the inside of the reactor was purged with nitrogen gas. While the inside of the reactor was heated at a rate of 1 °C per min to 145 °C from room temperature, hydrogen was fed at a rate of 100 sccm. The hydrogen was added at an amount twice as much as necessary for the reaction. The dimethyl (S)-malate prepared in Example 2 was dissolved in water to give a 30 wt% solution. This dimethyl (S)-malate solution was fed under the conditions shown in Table 1, below. Reaction products were taken every 9 hours and analyzed by gas

chromatography using a flame ionization detector  
(see page 13, the second paragraph).

TABLE 2

Example No.	Solvent	Conversion. (%)	Selectivity for (S)- HGB* (%)
9	30% H <sub>2</sub> O	92.0	85.5
10	20% H <sub>2</sub> O	94.0	72.0
11	10% H <sub>2</sub> O	95.0	78.0
12	10% i-PrOH	72.5	54.2

\* (S)-beta-hydroxy-γ-butyrolactone

(see page 15, the table 2).

This is identical with the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1625

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Taylor Victor Oh, MSD,LAC  
Primary Examiner  
Art Unit: 1625

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